Amdt. dated: May 6, 2004

Reply to Office Action of November 7, 2003

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

- (Currently amended) A method for increasing the proliferation of 1. thymocytes in a non-human animal comprising altering an endogenous gene encoding p27^{Kip1} in a somatic thymocyte, or a multipotent cell that differentiates into a thymocyte, of the animal to cause a functional deficiency of cyclin-dependent kinase inhibitor function of p27^{Kip1}, thereby increasing the proliferation of thymocytes in the animal.
- 2. (Currently amended) The method of claim 1, wherein the multipotent cell is a thymocyte or bone marrow cell.
- 3. (Original) The method of claim 1, wherein the animal is a rodent, pig, sheep, frog, or bovine.
- (Original) The method of claim 1, wherein the gene encoding p27^{Kip1} is altered by insertion of a positively selectable marker, mutation of the gene encoding p27Kipl, or deletion of the gene encoding p27^{Kip1}.
- (Original) The method of claim 4, wherein the gene encoding p27^{Kip1} is 5. altered by insertion of a positively selectable marker into the gene.
- 6. (Original) The method of claim 5, wherein the positively selectable marker encodes neomycin resistance, thymidine kinase, adenine phosphoribosyl transferase, hypoxanthine-guanine phosphoribosyl transferase or dihydrofolate reductase.
- 7. (Original) The method of claim 6, wherein the positively selectable marker encodes neomycin resistance.

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8. (Original) The method of claim 1, further comprising: introducing a plasmid into the cell, wherein the plasmid comprises the gene encoding p27^{Kip1} altered by insertion of a positively selectable marker.

- 9. (Currently amended) The method of claim 8, wherein the plasmid further comprises a negatively selectable marker adjacent the altered gene encoding p27^{Kip1}, whereby the distance between the negatively selectable marker and the altered gene encoding p27^{Kip1} is sufficient to allow homologous recombination between the altered gene encoding p27^{Kip1} and [[a]] the endogenous gene encoding p27^{Kip1} in the cell.
- 10. (Original) The method of claim 9, wherein the negatively selectable marker encodes thymidine kinase.
- 11. (Original) The method of claim 8, wherein the plasmid is delivered to the cell by electroporation, microinjection or transformation.